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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/818,954	03/27/2001	Christopher J.R. Paszty	A-676B	9125

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EXAMINER
SPECTOR, LORRAINE

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 11/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.

EXAMINER

ART UNIT	PAPER NUMBER
	11

DATE MAILED:

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 9/19/02

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-99 is/are pending in the application.
Of the above, claim(s) 9,12-46,52-60,62-64,66-99 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-8,10,11,47-51,61,65 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☒ Claim(s) 1-99 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 7 and 10
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

SEE OFFICE ACTION ON THE FOLLOWING PAGES

Part III: Detailed Office Action

Restriction Requirement:

Applicant's election with traverse of Invention I, claims 1-8, 10, 11, 47-51, 61 and 65, in Paper No. 9, filed 9/19/02 is acknowledged. The traversal is on the ground(s) that (1)the groups of inventions are not independent, and (2) the examination of the entire application would not constitute a burden to search. This is not found persuasive because with respect to point (1) above, the inventions are distinct as noted in the last Office Action, as shown by the distinctness described therein. Applicant's attention is directed to MPEP 806.05. With respect to point (2) above, contrary to applicants' assertion that any search of the prior art in regard to group I will reveal whether any prior art exists as to the other Groups, a search is directed to references which would render the invention obvious, as well as references directed to anticipation of the invention, and therefore requires a search of relevant literature in many different areas of subject matter.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-8, 10, 11, 47-51, 61 and 65 are under consideration. All other claims are withdrawn from prosecution as being drawn to non-elected inventions.

Formal Matters:

Claims 50 and 51 are objected to for depending from a non-elected claim. Correction is required.

Applicants are advised that the United States Patent and Trademark Office no longer requires identification of the algorithm used in claims that recite 'percent identity' of nucleic acid or protein sequences. Applicants may wish (but are not required) to cancel claim 11.

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an

affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973). The essential subject matter in question is the amino acid sequence of the subunit identified as α2, and referenced to WO 99/41377. As the claims require nucleic acids encoding α2, the sequence of such is considered to be essential to the claimed invention.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Double patenting rejections:

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

ABN

Claim 1 is provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of copending Application No. 09/723970. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 2-8, 10, 11, 47-51, 61 and 65 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8, 10, 11, 46-50, 61-67, 111 and 112 of copending Application No. 09/723970. Although the conflicting claims are not identical, they are not patentably distinct from each other because they differ only in the biological activity limitation, in that the current claims are more specific about the activity being in combination with an α2 subunit, however, the claims are coextensive and clearly drawn to one and the same β10 subunit.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Objections and Rejections under 35 U.S.C. §101 and §112:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-8, 10, 11, 47-51, 61 and 65 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility.

The specification discloses human and mouse nucleic acids encoding a putative protein which applicants name β10, due to its similarity to the β subunit of the glycoprotein hormones. At page 6 of the specification it is stated that the putative human protein has 31-37% identity to other human glycoprotein beta subunits. Suggested utilities for the claimed nucleic acids and protein are that various biological activities are *anticipated* as being attributable to the protein encoded by the claimed nucleic acids, based upon sequence similarity to the glycoprotein hormone beta subunits, and expression patterns (page 104), and that the nucleic acid and fusion proteins can be used for diagnosis and treatment of conditions associated with those activities. In addition, this application, which is a CIP of parent application 09/723970, discloses that transgenic mice which overexpress both the disclosed β10 and α2 subunits show bilateral thyroid enlargement with multiple follicular papillary adenomas and resultant hyperthyroidism, leading to the conclusion that "Thus in a normal mouse setting α2/β10 clearly has a TSH-like activity", and the anticipation that human β10 will have the same activity (see page 9 of the specification). None of these proposed uses represents a readily available, specific, substantial and credible utility.

Utility must be in readily available form. In Brenner v. Manson, 148 U.S.P.Q. 689 (Sup. Ct,.1966), a process of producing a novel compound that was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be useful because the compound produced thereby was potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The instant claims are drawn to a polynucleotide encoding a protein which has undetermined function or biological significance. Until some actual and specific activity can be

attributed to the protein identified in the specification as α2 protein or the polynucleotides encoding it, the claimed invention is incomplete. Merely using the polynucleotides to isolate other similar polynucleotides does not constitute a patentable utility.

The activity of α2/β10 heterodimers when overexpressed in transgenic mice does not confer utility to the claimed nucleic acids encoding β10. The overexpression of the two subunits in a transgenic animal is not predictive of the role of the β10 subunit *in vivo*. By virtue of the fact that, as disclosed at page 104 of the specification that β10 is expressed in brain, liver, fetal liver, stomach, pituitary, colon, small intestine, thyroid gland, adrenal gland, pancreas, skin, leukocytes, spleen, testis and placenta, the person of ordinary skill in the art would not accept as credible the assertion that the β10 subunit is merely another cytokine with 'TSH-like' activity. It remains that there is no known disease state or condition associated with β10. The overexpression study disclosed in the specification is not a valid means of determining what the actual *in vivo* role of the disclosed β10 subunit is. Many cytokines will have different effects when overexpressed than they do when expressed at naturally occurring levels by cell types that naturally express them. The transgenic mice disclosed in the specification are engineered to overexpress the α2/β10 heterodimer "in their circulation" (page 150). Given the list of tissues that are known to express β10 (above), such is not predictive of the *in vivo* activity of the subunit; its primary role would not seem to be to exist in high levels 'in their circulation'. Also, it is not predictable that α2 is the subunit with which the β10 subunit naturally combines *in vivo*. Finally, the transgenic experiment does not, in and of itself, present any readily available utility for the β10 subunit or nucleic acids encoding such. While applicants have certainly further characterized the β10 subunit since the filing of the parent application, that characterization has not progressed to the point of constituting a disclosure of a specific, substantial and credible utility that is readily available. It remains that the disclosure presents an invitation to experiment to find a use for the disclosed nucleic acids.

With regard to diagnosis or treatment of conditions associated with expression of the β10 protein or encoding nucleic acids, such does not constitute as substantial assertion in the absence of any known disease or condition which could be so treated, but merely represents an invitation to

experiment to discover such diseases or conditions.

Accordingly, the Examiner finds that there is no readily available specific, substantial and credible use for the claimed nucleic acids.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, 10, 11, 47-51, 61 and 65 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claims 1-8, 10, 11, 47-51, 61 and 65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification as originally filed provides a written description only of a single protein identified as β10 and nucleic acids encoding such. The claims however, broadly encompass allelic variants, splice variants, orthologs, or naturally occurring variants. Further, claims such as claim 1 encompass nucleotide sequences which are characterized only by the ability to hybridize to a nucleic acid encoding β10, and encoding a polypeptide with 'an activity' of β10, which activities are themselves not described in the specification as filed. There is no written description of such variants, nor has the gene disclosed and named β10 been described in a manner that would constitute

a written description of such, e.g. what the critical features of β10, are in a manner that would convey that the inventor had possession of the invention in a manner commensurate with the scope of the claims at the time the invention was made.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of the sequences referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only nucleic acids of SEQ ID NO: 2 or which encode SEQ ID NO: 1 or 3, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8, 10, 11, 47-51, 61 and 65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims which recite "moderately" or "highly" stringent conditions, such as claims 1-3, are indefinite because there is no limiting definition of such in the specification, and the metes and bounds of that which will hybridize are dependent upon the conditions under which the hybridization is performed. The discussion of such at pages 31-33 of the specification is noted but vague, fails to breathe life and meaning into the term, is exemplary rather than limiting, and thus is insufficient to render the claims definite.

Claim 2 is further indefinite at part (d) of the claim, as the nature of the 'fragment of at least 16 nucleotides' is not clear. This also applies to other claims, for example claim 3, part (f).

Claim 3 is further indefinite for failing to adequately point out that which applicant sees as the invention. There is no upper limit to the number of substitutions, insertions, deletions, or truncations, such that there is no requirement for any structural similarity to the disclosed nucleic acids.

Claim 8 is also further indefinite for failing to adequately point out that which applicant sees as the invention: The claim recites that it is a β10 polypeptide that is to be produced, whereas the claims from which it depends do not provide antecedent basis for the recitation of "β10 polypeptide", nor does the specification adequately breathe life and meaning into the term such that the metes and bounds of the claim can be discerned. Simply put, it is not clear what the identifying characteristics of a "β10 polypeptide" are.

Claim 10 is further indefinite as there is no written description of a "native β10 polypeptide" promoter, such that the metes and bounds of the claim cannot be determined, even in light of the specification. Similarly, claim 61 is indefinite as the metes and bounds of "human β10 polypeptide"

are not clear.

All claims are indefinite as the metes and bounds of "α2" cannot be determined.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

X Claims 1-5, 7 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by, or in the alternative under 35 U.S.C. § 103(a) as being obvious over G.G. Mahairas et al., Locus AQ495547 disclosed 4/28/99.

G.G. Mahairas et al. disclose Locus AQ495547, which has 100% identity to basses 22-209

of SEQ ID NO: 2. Because that nucleic acid would inherently hybridize to that of SEQ ID NO: 2 and encode a polypeptide with at least one activity of the polypeptide encoded by SEQ ID NO: 2, it meets the limitations of claim 1, and given the formulae for calculating percent identity in the specification (page 20, line 30) also meets the limitations of claim 2, and is truncated, meeting the limitations of claim 3. The nucleic acid was cloned into a pBACe3.6 vector, bacterial artificial chromosome, hence the vector was necessarily propagated in prokaryotic (bacterial) cells.

The claims require that "the encoded polypeptide, when heterodimerized to human α2 polypeptide, has an activity of the human α2/β10 heterodimer. The examiner is unable to determine whether the prior art disclosure possesses the unrecited characteristics or property. The nucleic acid of Mahairas encodes residues 8-70 of the protein of SEQ ID NO: 1, however, it cannot be determined whether this is sufficient to heterodimerize with α2, nor what the characteristics of such heterodimer would be, although it is fairly certain that it would at least have the activity of β10 of comprising at least one antibody-binding epitope of such. With these conditions, where the product seems to be identical except that the prior art is silent to the characteristic or property claimed, then the burden shifts to applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention. Note the case law of *In re Best* 195 USPQ 430, 433 (CCPA 1977).

Claims 6, 8, and 48-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mahairas et al., locus AQ495547, as cited above, in view of Sibson et al., WO94/01548.

The rejected claims require a eukaryotic host cell (claims 6 and 65), expression of the encoded protein (claims 8 and 66) using a heterologous promoter (claim 9), production of a fusion protein (claims 49 and 111), said fusion to IgG or a variant thereof (claim 50 and 112).

The teachings of Mahairas et al. are summarized above. None of the aforementioned limitations are taught or suggested by Mahairas et al.

Sibson et al. disclose that it is generally useful to place a desired cDNA sequence into an expression vector, host cell, and express the encoded protein, as well as to raise antibodies to proteins encoded

by such cDNA's. See pages 8-13. Expression in eukaryotic cells, and the advantages thereof, are discussed at page 9, first paragraph. Fusion proteins are also taught, see page 11, lines 15-15 and 26-29.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use the DNA's disclosed by the primary reference to express and then isolate the encoded polypeptide using a heterologous promoter, to make a fusion protein of such, and to express such in eukaryotic cells, using a viral vector, all as taught by Sibson et al. in view of Sibson et al.'s suggestion that it would be desirable to do so, as cited above.

Advisory Information:

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz, at (703)308-4623.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to (703) 746-5228.

Lorraine Spector

Lorraine Spector, Ph.D.
Primary Examiner

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